

That Which Is Claimed Is:

1. A composition comprising infectious alphavirus particles in an immunogenic effective amount, wherein said alphavirus particles comprise one or more
5 heterologous nucleotide sequences encoding an antigen; and wherein said antigen is selected from the group consisting of a native cancer cell antigen and an artificial cancer antigen that is not normally expressed by a cancer cell.

2. The composition of Claim 1, wherein said alphavirus particle is an
10 alphavirus replicon particle.

3. The composition of Claim 1, wherein said alphavirus is a Venezuelan Equine Encephalitis virus.

4. The composition of Claim 1, wherein said alphavirus comprises one or
15 more attenuating mutations.

5. The composition of Claim 3, wherein said alphavirus comprises one or
20 more attenuating mutations.

6. The composition of Claim 5, wherein at least one of said one or more
attenuating mutations is selected from the group consisting of codons at E2 amino acid
position 76 which specify an attenuating amino acid, codons at E2 amino acid
position 120 which specify an attenuating amino acid, codons at E2 amino acid
25 position 209 which specify an attenuating amino acid, codons at E1 amino acid 272
which specify an attenuating mutation, codons at E1 amino acid 81 which specify an
attenuating mutation, and codons at E1 amino acid 253 which specify an attenuating
mutation, and the deletion of E3 amino acids 56-59.

7. The composition of Claim 1, wherein each of said one or more
30 heterologous nucleotide sequences is operably associated with a promoter.

8. The composition of Claim 7, wherein said promoter operably associated with each of said one or more heterologous nucleotide sequences is an alphavirus 26S subgenomic promoter.

9. The composition of Claim 1, wherein at least one of said one or more nucleotide sequences encodes a native cancer cell antigen.

10. The composition of Claim 1, wherein at least one of said one or more nucleotide sequences encodes an artificial cancer antigen that is not normally expressed by a cancer cell.

11. The composition of Claim 10, wherein said artificial cancer antigen is an infectious disease antigen.

12. The composition of Claim 11, wherein said infectious disease antigen is an influenza hemagglutinin antigen.

13. The composition of Claim 10, wherein said at least one nucleotide sequence encoding an antigen is selected from the group consisting of helper T cell epitopes, cytotoxic T cell epitopes, T-dependent B cell epitopes, and T-independent B cell epitopes.

14. The composition of Claim 1, wherein at least one of said one or more nucleotide sequences encodes a cell-surface protein or peptide.

15. A pharmaceutical formulation comprising the composition of Claim 1 in a pharmaceutically acceptable carrier.

16. A kit for modifying a mammalian cell, comprising:
(a) assay components for determining the pre-existing immunity of a subject afflicted with cancer to one or more antigens; and
(b) one or more vectors suitable for introducing and expressing an antigen in a mammalian cell, each of said vectors comprising one or more

Sub A
heterologous nucleotide sequence(s) encoding an antigen from said one or more antigens.

17. A method for inducing a protective immune response in a subject
5 afflicted with cancer, comprising:

(a) modifying a cell to express one or more antigens against which the subject has a pre-existing immunity; and

(b) introducing the modified cell into the subject, wherein the modified cell elicits an immune response against the subject's cancer.

10

18. A method for inducing a protective immune response in a subject afflicted with cancer, comprising:

(a) screening a subject afflicted with cancer for pre-existing immunity against one or more antigens;

15

(b) selecting one or more antigens against which the subject demonstrates immunity;

(c) modifying a cell to express the one or more selected antigens; and

20

(d) introducing the modified cell into the subject, wherein the modified cell elicits an immune response against the subject's cancer.

19. The method of Claim 18, wherein the subject's cancer cells and the modified cell share at least one antigen native to the subject's cancer cells.

25

20. The method of Claim 18, wherein the cancer is a tumor-forming cancer.

30

21. The method of Claim 18, wherein the cell to be modified is removed from the subject.

22. The method of Claim 21, wherein the cell to be modified is a cancer cell.

23. The method of Claim 18 further comprising the step of immunizing the subject against at least one of the one or more selected antigens.

24. The method of Claim 23, wherein said immunizing step is carried out prior to said introducing step.

25. The method of Claim 23 further comprising a second step of immunizing the subject against at least one of the one or more selected antigens.

26. The method of Claim 25, wherein said immunizing step and said second immunizing step each use a different vector.

27. The method of Claim 18, wherein said immunizing step is carried out with an alphavirus vector.

28. The method of Claim 27, wherein the alphavirus is a Venezuelan Equine Encephalitis virus.

29. The method of Claim 18, wherein the subject is a human subject.

30. The method of Claim 18, wherein the pre-existing immunity is the result of childhood vaccination.

31. The method of Claim 18, wherein at least one of the one or more selected antigens are not typically expressed by the subject's cancer cells.

32. The method of Claim 31, wherein the at least one selected antigen is an infectious disease antigen.

33. The method according to Claim 32, wherein the infectious disease antigen is selected from the group consisting of influenza antigens, polio antigens, herpes antigens, mumps antigens, measles antigens, rubella antigens, diphtheria toxin, other diphtheria antigens, pertussis antigens, and hepatitis antigens.

34. The method of Claim 18, wherein at least one of said one or more selected antigens is a cell surface protein or peptide.

5 35. A method for inducing a protective immune response against cancer in a subject, comprising:

- (a) immunizing a subject against one or more antigens prior to the detection of cancer in the subject;
 - (b) modifying a cell to express the one or more antigens of (a); and
 - (c) introducing the modified cell into the subject, wherein the
- 10 modified cell elicits an immune response against the subject's cancer.

36. The method of Claim 35, wherein the cancer is a tumor-forming cancer.

15 37. The method of Claim 35, wherein the cell to be modified is removed from the subject.

38. The method of Claim 37, wherein the modified cell is a cancer cell.

20 39. The method of Claim 35 further comprising a second step of immunizing the subject against the one or more antigens.

40. The method of Claim 39, wherein said second immunizing step is carried out prior to said introducing step.

25 41. The method of Claim 39, wherein said second immunizing step is carried out with an alphavirus vector.

42. The method of Claim 35, wherein the subject is determined to be at

30 risk for the development of cancer.

43. The method of Claim 35, wherein at least one of the one or more antigens is not normally expressed by the subject's cancer cells.

44. The method of Claim 43, wherein the at least one antigen is an infectious disease antigen.

5 45. The method of Claim 44, wherein the at infectious disease antigen is selected from the group consisting of influenza antigens, polio antigens, herpes antigens, mumps antigens, measles antigens, rubella antigens, diphtheria toxin, other diphtheria antigens, pertussis antigens, and hepatitis antigens.

10 46. The method of Claim 43, wherein the at least one antigen is selected from the group consisting helper T cell epitopes, cytotoxic T cell epitopes, T-dependent B cell epitopes, and T-independent B cell epitopes.

15 47. The method of Claim 35, wherein at least one of the one or more antigens is a native cancer antigen.

48. The method of Claim 35, wherein at least one of said one or more antigens is a cell-surface protein or peptide.

20 49. A method for inducing a protective immune response against cancer in a subject, comprising immunizing a subject against an antigen prior to the detection of cancer in the subject, wherein said immunizing step is carried out using an alphavirus vector comprising a nucleotide sequence encoding the antigen.

25 50. The method of Claim 49, wherein said alphavirus vector is an alphavirus replicon particle vector.

51. The method of Claim 49, wherein said alphavirus vector is a Venezuelan Equine Encephalitis virus vector.

30 52. The method of Claim 49 further comprising a second step of immunizing the subject against the antigen.

53. The method of Claim 52, wherein said immunizing step and said second immunizing step are carried out with different alphavirus vectors.

54. The method of Claim 49, wherein the subject is one determined to be at risk for the development of cancer.

55. The method of Claim 49, wherein the antigen is not normally expressed by the subject's cancer cells.

56. The method of Claim 55, wherein the antigen is an infectious disease antigen.

57. The method of Claim 49, wherein the antigen is a native cancer antigen.

58. A method for inducing a protective immune response against cancer in a subject, comprising:

- (a) immunizing a subject afflicted with cancer against one or more antigens;
- (b) modifying a cell to express the one or more antigens of (a); and
- (c) introducing the modified cell into the subject, wherein the modified cell elicits an immune response against the subject's cancer.

59. The method of Claim 58, wherein the cancer is a tumor-forming cancer.

60. The method of Claim 58, wherein the cell to be modified is removed from the subject.

61. The method of Claim 60, wherein the cell is a cancer cell.

62. The method of Claim 58 further comprising a second step of immunizing the subject against at least one of the one or more antigens.

63. The method of Claim 62, wherein said second immunizing step is carried out prior to said introducing step.

64. The method of Claim 63, wherein different vectors are used for said immunizing step and said second immunizing step

5 65. The method of Claim 58, wherein said immunizing step is carried out with an alphavirus vector.

66. The method of Claim 65, wherein the alphavirus is a Venezuelan Equine Encephalitis virus.

10 67. The method of Claim 58, wherein at least one of the one or more antigens is not normally expressed by the subject's cancer cells.

15 68. The method of Claim 67, wherein the at least one antigen is an infectious disease antigen.

69. The method of Claim 58, wherein at least one of the one or more antigens is a native cancer antigen.

20 70. A method for inducing a protective immune response against cancer, comprising the step of immunizing a subject against a native cancer antigen, wherein said immunizing step is carried out using an alphavirus vector comprising a nucleotide sequence encoding a native cancer antigen.

25 71. The method of Claim 70, wherein said alphavirus vector is an alphavirus replicon particle vector.

72. The method of Claim 70, wherein said alphavirus is a Venezuelan Equine Encephalitis virus.

30 73. The method of Claim 70, wherein said subject is determined to be at risk for the development of cancer.

74. ~~The method of Claim 70, further comprising a second step of immunizing the subject against the native cancer antigen.~~

75. ~~The method of Claim 74, wherein different alphavirus vectors are used for said immunizing step and said second immunizing step.~~

76. ~~The method of Claim 70, wherein said immunizing step is carried out before the detection of cancer in the subject.~~

77. ~~The method of Claim 70, wherein said second immunizing step is carried out before the detection of cancer in the subject.~~

78. ~~The method of Claim 74, wherein said second immunizing step is carried out after the detection of cancer in the subject.~~

79. ~~A method for inducing an immune response against a native cancer antigen, comprising the step of immunizing a subject afflicted with cancer against an antigen native to the subject's cancer, wherein said immunizing step is carried out using an alphavirus vector comprising a nucleotide sequence encoding an antigen native to the subject's cancer.~~

80. ~~The method of Claim 79, wherein the alphavirus vector is an alphavirus replicon particle vector.~~

81. ~~The method of Claim 79, wherein said alphavirus is a Venezuelan Equine Encephalitis virus.~~

82. ~~The method of Claim 79, further comprising a second step of immunizing the subject against the antigen native to the subject's cancer.~~

83. ~~The method of Claim 82, wherein different alphavirus vectors are used for said immunizing step and said second immunizing step.~~

~~Handwritten scribbles and markings at the bottom left of the page.~~

add
B3
x
B4

add
add C1
add B3
add F4